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Trauma Induced Coagulopathy

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Stem Case and Key Questions Content

A 28-year-old male is admitted to the emergency department after being struck by a motor vehicle travelling at a 35 mile per hour. At the time of admission, he is combative and agitated and reports that he had been drinking at a friend's house earlier in the evening. Upon arrival he is noted to have a blood pressure of 90/70 mm Hg, heart rate of 120 beats/min, and arterial oxygen saturation on room air of 90%. There are obvious deformities of the Left arm and left thigh with a large laceration over the forehead. He also complains of significant pain with manipulation of the pelvis which appears to be unstable. His skin is noted to be cool and clammy with difficulty in obtaining a pulse oximetery reading. His temperature is 35.6 oC.

KEY QUESTION #1: What are the immediate priorities in the early management of a trauma patient?
KEY QUESTION #2: What would you choose as the initial resuscitative fluid and how much would you give?

The patient is intubated and additional intravenous access is obtained. Resuscitation is initiated with packed red blood cells (PRBC). A focused assessment by sonography in trauma (FAST) exam is performed at the bedside and shows free fluid in the abdomen. The patient's blood pressure is now 78/40 mm Hg with a heart rate of 118 beats/min.

KEY QUESTION #3: What would be the next step in the management?
KEY QUESTION #4: Is he ready for the operating room?

As you are going to the operating room (OR), the initial laboratory data becomes available: hematocrit 29%, platelets 170,000, lactate 4.5, and international normalized ratio (INR) 3.4. An arterial blood gas shows: PaO2 125 mm Hg, PaCO2 36, and pH 7.15. The patient's blood pressure despite ongoing resuscitation is now 68/40 mm Hg.

KEY QUESTION #5: What type of resuscitative fluids would you use?
KEY QUESTION #6: Can you explain the coagulopathy on admission?
KEY QUESTION #7: How would you address the coagulopathy?

In the operating room, the patient is found to have significant hemoperitoneum with a Grade IV splenic laceration, a Grade III liver laceration, and two mesenteric tears. A damage control approach is taken with his surgical management including splenectomy, bowel resection, packing of the abdomen, and placement of external fixation for his fractures. He has received 20 U of PRBC, 22 U of fresh frozen plasma (FFP), and 3 packs of platelets. His INR is 2.2 and

lactate is now 5.2. He appears to still have diffuse bleeding and the surgeon is concerned about his ongoing coagulopathy.

KEY QUESTION #8: How would you address the surgeon's concern? How would you treat the patient's coagulopathy?

The patient is administered additional platelets, cryoprecipitate, and Factor VII with significant reduction in his ongoing blood loss. He is taken to the interventional radiology suite where he undergoes coiling of some pelvic vessels with active extravasation. He is admitted to the intensive care unit.

KEY QUESTION #9: What is your ultimate goal in correcting the trauma induced coagulopathy

Model Discussion Content

Initial management of the trauma patient still focuses on the ABC's; airway, breathing and circulation with an emphasis on hemorrhage control at all phases of the initial evaluation and treatment. In the trauma patient who is hypotensive on admission with evidence of altered mental status and a high likelihood of early operative interventions, early intubation may be indicated. Additionally, large bore intravenous access must be achieved and can include the placement of central venous access provided this does not unduly delay emergent care compared to obtaining peripheral access. If a patient presents with a systolic blood pressure of less than 90 mm Hg, evidence of poor perfusion and a positive FAST for intra-abdominal fluid, he would be a candidate for "damage control resuscitation". Packed red blood cells would be an acceptable choice during the initial resuscitation with concomitant administration of FFP. In the presented hypothetical scenario, the patient would be a candidate for immediate transfer to the operating room for an exploratory laparotomy in addition to placement of external fixation for his humeral and femur fractures. In contrast to previous approaches that emphasized early aggressive administration of crystalloids to assess fluid responsiveness in the hypotensive trauma patient, many centers have switched to early blood product usage, particularly if the circumstances warrant a "damage control resuscitation".[1]

Damage control resuscitation (DCR) "is a treatment strategy that targets the conditions that exacerbate hemorrhage in trauma patients".[1] While many components of this approach have not been evaluated through randomized controlled trials, DCR embodies significant expert opinion along with multiple studies targeting the management of the trauma patient requiring massive transfusion. The key elements of this approach include the integration of DCR with damage control surgery, transfusion ratios, permissive hypotension, avoidance of isotonic crystalloid fluids, and aggressive management of hypothermia, acidosis, and coagulopathy. While all of these elements are important in the resuscitation of the trauma patient with massive bleeding, we will focus on the impact of coagulopathy in the setting of trauma. Trauma-induced coagulopathy (TIC) is multifactorial and encompasses all components of the hemostatic system. TIC is specifically associated with the extent and severity of tissue trauma, and correlates with mortality. This coagulopathy can be present on admission in one in four trauma patients and is associated with a 4-fold increase in mortality.[2] There appear to be eight key factors in the development of TIC: shock/inflammation, hemodilution, consumption, hyperfibrinolysis, acidosis, hypothermia, anemia and electrolyte disturbances.[2,3]

Because of evidence that severely injured trauma patients are likely to develop TIC, an early and aggressive endogenous coagulopathy, separate from later loss and dilution of clotting factors compounded from hypothermia and acidosis,[4-10] the practice of “hemostatic” resuscitation has become commonplace in the most severely injured patients. This entails the early and aggressive use of hemostatic products combined with red blood cells as the primary resuscitation fluids in order to avoid rapid deterioration into the “bloody vicious cycle” and the classic “lethal triad” of hypothermia, acidosis and coagulopathy.[11] Two very distinct paradigms of hemostatic resuscitation have currently emerged: the DCR model, which uses pre-emptive administration of empiric ratios of blood and hemostatic products to approximate whole blood, often according to an established institutional “massive transfusion protocol”;[1,12-15] and goal-directed hemostatic resuscitation approaches (also often protocol-based), which generally use point-of-care viscoelastic monitoring combined with the prompt administration of hemostatic concentrates.[16-19] Regardless, it is highly likely that the patient with massive hemorrhage and a coagulopathy has been managed according to some sort of hemostatic resuscitation approach which should be continued in the OR and postoperative period until it is clear that hemostasis has been achieved. It is important the anesthesiologist communicate with the trauma team to see where the patient is in terms of their hemostatic resuscitation.

The majority of trauma patients initially present with normal or pro-thrombotic coagulation profiles. However, those most seriously injured are likely to present with evidence of hypocoagulability, accelerated fibrinolysis, or both.[16,20] It is essential therefore to promptly re-assess the patient’s coagulation status in order to initiate appropriate therapy. “Standard” laboratory tests such as prothrombin time (PT), partial thromboplastin time (PTT), INR, fibrinogen level and platelet count are still the most common coagulation assays in clinical use, despite considerable evidence that they provide an extremely incomplete picture of in vivo hemostasis,[17,18] that they are poor predictors of clinical bleeding,[21] and that they do not provide an adequate basis for rational targeted hemostatic resuscitation.[22,23] Although significantly elevated admission PT and PTT levels are predictive of increased mortality from injury,[5] there is little evidence that they provide a realistic target for resuscitation. Moderately elevated values may have little clinical significance, and correction to “normal” values may require large amounts of resuscitation fluids, especially fresh frozen plasma (FFP). Absent evidence of active clinical bleeding, “chasing” these may do more harm than good.

These deficiencies underscore the need for reliable point-of-care hemostatic monitoring with clinical relevance in situations of generalized coagulopathy due to massive hemorrhage. There is increasing evidence that viscoelastic monitoring technologies such as TEG® (Haemonetics Corp., Niles, IL, USA) and ROTEM® (Tem Innovations GmbH, Munich, Germany) are superior for detecting clinically relevant hemostatic abnormalities in trauma and surgical patients with massive bleeding and diffuse coagulopathy.[17,24,25] Viscoelastic monitoring has been much more widely used in Europe than in the United States, but is seeing increased usage for early assessment in intra-operative and ICU management of bleeding surgical and trauma patients,. It should also be noted that both viscoelastic and standard coagulation tests are generally performed after warming specimens to 37oC, and do not reflect the potentially considerable effects of hypothermia on in vivo hemostasis.[26]

With DCR, large volumes of fresh frozen plasma are frequently administered as part of the hemostatic resuscitation and this aggressive use of FFP may be continued into the ICU setting.

In a recent study, Stanworth and colleagues looked at the use of FFP in ICUs in Great Britain and found considerable variation, including frequent administration in the absence of clinical bleeding and even in the absence of PT prolongation.[27] The amounts administered to bleeding patients were generally well below the levels shown by Chowdhury to be necessary.[28] Not surprisingly, post-transfusion correction of INR values was generally small.

More aggressive correction may substantially increase the risks of adverse complications. One study attempting to correct the INR to 1.3 in the ICU documented a high rate of severe ARDS.[29,30] If FFP is being used as the primary hemostatic resuscitation fluid and viscoelastic monitoring is not available, the anesthesiologist should generally accept an INR in the 1.5-1.8 range provided there is no evidence of active bleeding. Isolated PT/INR levels are poor predictors of clinical bleeding in trauma patients, and thrombin generation is generally preserved or even increased after significant blood loss because of dysregulation, with loss of clotting factors balanced by loss of regulatory inhibitors.[31]

Recombinant activated factor VIIa (rFVIIa) has found considerable off-label use in the management of refractory coagulopathy in hemorrhagic shock/trauma patients. Although initially touted as a “total hemostatic agent”, it now seems clear that rFVIIa acts mainly as a potent thrombin generator.[32] High dose rFVIIa (usually >= 80-90 mcg/kg) works predominantly by a direct effect on activated platelets rather than via its higher affinity binding to tissue factor.[33]

Because tissue factor is expressed by inflammatory cells, there is significant potential for systemic micro-thrombi generation, and several studies have shown a risk of thrombotic complications on the order of 5-7%.[34] Efficacy of rFVIIa is dependent on the presence of adequate substrate for clot formation such as fibrinogen and platelets, and may be significantly impaired under acidotic conditions.[35] Because of these considerations, the use of high dose rFVIIa as rescue therapy in refractory hemorrhagic shock is controversial, and should be undertaken with caution. Earlier use of lower dose rFVIIa combined with adequate substrate replacement may be a safer and more efficacious approach. The anesthesiologist should be aware that patients who have received rFVIIa during their resuscitation may have a normal INR, but this may only be a transient finding.

Finally, fibrinolysis is especially deleterious in severely injured trauma patients and carries an associated mortality well upwards of 50%.[16,36,37] The majority of patients with primary fibrinolysis from severe hemorrhagic shock may never survive to the ICU. The recently concluded CRASH-2 trial is the only class I evidence to date showing a 30 day survival benefit for a resuscitative therapy.[38] Subgroup analysis showed that the benefit was greatest when therapy was instituted within 1 hour of admission. However, subgroup analysis showed that mortality actually increased when therapy was instituted after 3 hours, suggesting that the risks of therapy outweighed the benefits in patients who survived beyond that timeframe.[39] It may therefore be prudent to carefully consider administering the anti-fibrinolytic therapy as early as possible in the Trauma patient who is bleeding or at risk of significant hemorrhage.[40] Also, carefully assessing the risks of giving it past the 3 hour window, even if the patient has laboratory evidence of fibrinolysis.

In summary, the anesthesiologist must be aggressive about treating ongoing clinical coagulopathy in severely injured patients, but must also be aware of the risks and benefits of hemostatic agents and avoid over-aggressive treatment, particularly as the patient converts to a

pro-thrombotic state. There are considerable data indicating that standard coagulation tests may not correlate well with clinical bleeding, and “chasing” a laboratory value may result in deleterious over-administration of coagulation products. Whether DCR (an empiric/ratio-based transfusion strategy) or goal-directed protocols are used, care should be taken to correlate therapy with evidence of clinical bleeding and to discontinue hemostatic treatment once endpoints have been met. Viscoelastic monitoring appears to be a more accurate measure of clinical coagulopathy in critically injured patients, and will likely become increasingly utilized in the acute and intraoperative management of TIC.

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